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EXAMINER	
UNGAR, SUSAN NMN	

ART UNIT	PAPER NUMBER
1642	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/071,838	LI ET AL.	
	Examiner	Art Unit	
	Susan Ungar	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *26 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-43* is/are pending in the application.

4a) Of the above claim(s) *10-43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/6/02, 12/2/02, 3/29/04*
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☑ Other: Appendix 1

1. The Election filed November 26, 2004 in response to the Office Action of September 20, 2004 is acknowledged and has been entered. Claims 1-43 are pending in the application and Claims 10-43 have been withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to non-elected inventions. Claims 1-9 drawn to a method of detecting cancer cells comprising detecting a nucleic acid molecule encoding SEQ ID NO:2 are currently under prosecution.

2. Applicant's election with traverse of Group 1, claims 1-9 is acknowledged. Applicant argues that where claims can be examined together without undue burden, the Examiner must examine the claims on the merits even though they are directed to independent and distinct inventions. Applicant submits that a proper search of the claims drawn to detection of cancer by detecting nucleic acid and amino acid sequences relating to SEQ ID NO;2 would not constitute an undue burden since a proper search would likely encompass both nucleic acid and protein sequences. The argument has been considered but has not been found persuasive because the literature search, particularly relevant in this art, is not coextensive and different searches and issues are involved in the examination of each group. Further, Applicant argues that a proper search would also likely detect art relating to both detecting and monitoring the efficacy of cancer treatment and therefore Applicant requests that Groups 1-4, 13-16, 25-28, 37-40 be rejoined. The argument has been considered but has not been found persuasive because the literature search, particularly relevant in this art, is not coextensive and different searches and issues are involved in the examination of each group. For these reasons the restriction requirement is deemed to be proper and is therefore made FINAL.

In addition, Applicant argues that the division of claim 1-9 into four groups based on the type of cancer detected is contrary to MPEP and Applicant specifically

states that the proper practice is to issue a species election requirement and not a restriction. The argument has been considered and upon the examination of the claims, it was found that there is no undue burden in examining Groups 1-4 drawn to four different types of cancer, therefore, the inventions of Groups 1-4, claims 1-9 are hereby rejoined.

Specification

3. The specification on page 1 should be amended to reflect the status of the parent application.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

"The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention."

5. Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to a method of detecting cancer in a biological sample from a mammal comprising the steps of providing a biological sample from the mammal and detecting a nucleic acid molecule encoding a PRC17 polypeptide comprising at least 85% identity to an amino acid sequence of SEQ ID NO:2, wherein said polypeptide has an amino acid sequence of SEQ ID NO:2, wherein an increase in the level of said nucleic acid in the sample compared to normal indicates the presence of cancer cells.

The specification teaches that nucleic acids encoding a PRC17 polypeptide, including a full-length PRC17 protein or any derivative, variant, homolog or fragment thereof is useful for diagnostic assays (p. 23, lines 17-24). The specification teaches that PRC17 polynucleotides will be detected using art known techniques such as RT-PCR (p.25, lines 6-12). The specification exemplifies the amplification and overexpression of a PRC17 polynucleotide in Example 1, pages 56-58 wherein it is disclosed that the PCR17 gene is amplified in some primary prostate, breast, ovary samples and that PCR17 mRNA is overexpressed in primary prostate, metastatic prostate, breast, lung and ovary tumor samples (p. 58, see Table 3). However, it is noted that there is no nexus established between a polynucleotide encoding SEQ ID NO:2 and the overexpressed and/or amplified polynucleotides. The specification further teaches that similar studies were carried out to analyze overexpression of PRC17 Splice Variant 1. However, no data drawn to the overexpression of the splice variant is included in the specification as originally filed.

One cannot extrapolate the teaching of the specification to the enablement of the claims because it is not possible to determine the identity of the PCR17 polynucleotide that is overexpressed and/or amplified. The specification appears to exemplify the specific overexpression and/or amplification of a single PCR17 polynucleotide but does not provide any nexus between the overexpressed and/or amplified PCR17 polynucleotide and a polynucleotide encoding SEQ ID NO:2 or any other specific polynucleotide for that matter. In addition, withdrawn from consideration are two additional PCR17 polynucleotides and it cannot be determined from the information in the specification which of the polynucleotides is in fact overexpressed or amplified in the cancers samples exemplified. In particular, it cannot be determined whether the assayed polynucleotide is the polynucleotide

encoding SEQ ID NO:2 or whether it is that polynucleotide that is overexpressed and/or amplified in the primary tumors exemplified. Further, it cannot be determined if the polynucleotide encoding SEQ ID NO:2 is in fact Splice Variant 1 that is disclosed, but apparently is not overexpressed since no data is provided drawn to the Splice Variant.

The specification provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predictably determine whether a polynucleotide encoding SEQ ID NO:2 is in fact overexpressed and/or amplified and in the absence of that information, one would not be able to make or use the claimed invention with a reasonable expectation of success.

6. If Applicant were able to overcome the rejection set forth above, Claims 1-9 would still be rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of detecting cancer in a biological sample from a mammal comprising the steps of providing the biological sample from the mammal and detecting a nucleic acid encoding SEQ ID NO:2, wherein an increase in the level of SEQ ID NO:1 in the sample compared to normal indicates the presence of cancer cells, does not reasonably provide enablement for a method of detecting cancer in a biological sample from a mammal comprising the steps of providing the biological sample from the mammal and detecting a nucleic acid molecule encoding a PRC17 polypeptide comprising at least 85% identity to an amino acid sequence of SEQ ID NO:2, wherein said polypeptide has an amino acid sequence of SEQ ID NO:2, wherein an increase in the level of said nucleic acid in the sample compared to normal indicates the presence of cancer cells. The specification does not enable any

person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims.

The claims are drawn to a method of detecting cancer in a biological sample from a mammal comprising the steps of providing a biological sample from the mammal and detecting a nucleic acid molecule encoding a PRC17 polypeptide comprising at least 85% identity to **an** (emphasis added) amino acid sequence of SEQ ID NO:2, wherein said polypeptide has **an** (emphasis added) amino acid sequence of SEQ ID NO:2, wherein an increase in the level of said nucleic acid in the sample compared to normal indicates the presence of cancer cells. This means detecting cancer cells by detecting a nucleic acid molecule that encodes a PRC17 polypeptide, wherein said PRC17 polypeptide is defined by the specification as including polymorphic variants, mutants, interspecies homologs that have at least 85% identity to a region of about 20 or more amino acids of SEQ ID NO:2 (p. 26), wherein it is noted that the specification does not require that the amino acids be contiguous and which means that a PRC17 polypeptide is any polypeptide with 17 amino acids in common with PRC17 over a range of 20 amino acids.

The specification teaches that nucleic acids encoding a PRC17 polypeptide, including a full-length PRC17 protein or any derivative, variant, homolog or fragment thereof is useful for diagnostic assays (p. 23, lines 17-24). The specification teaches that PRC17 polynucleotides will be detected using art known techniques such as RT-PCR (p.25, lines 6-12). The specification exemplifies the amplification and overexpression of a PRC17 polynucleotide in Example 1, pages 56-58 wherein it is disclosed that PCR17 gene is amplified in some primary prostate, breast, ovary samples and that PCR17 mRNA is overexpressed in primary prostate, metastatic protstate, breast, lung and ovary tumor samples (p. 58, see Table 3).

One cannot extrapolate the teaching of the specification to the scope of the claims because the isolation of a single unidentified PCR17 gene that is overexpressed and/or amplified in a variety of primary tumors does not predictably enable the broadly claimed invention. Although the claims are clearly drawn to assaying nucleic acids encoding derivatives, variants, homologs of SEQ ID NO:2 and thereby detecting cancer cells, the specification provides no teachings that any polynucleotide other than the exemplified PCR17 gene is in fact either overexpressed or amplified in cancer cells. In particular, Pollack et al (Nature Genetics, 1999, 23:41-46, IDS item) specifically teaches that in an assay of 3195 genes it was found that most genes in cancer cells are not either amplified or overexpressed (see Figure 5, page 44) and that most highly expressed genes are not amplified, and not all amplified genes are highly expressed (p. 45, col 1). Thus, in the absence of further guidance in the specification, it cannot be determined which or whether any of the broadly claimed species to be assayed are in fact either amplified or overexpressed and one would not be able to predictably use the claimed invention.

In addition, the specification provides no information as to a structure that is common to the overexpressed/amplified PCR17 encoding gene that can be used to predictably distinguish between the PCR17 encoding genes that are overexpressing/amplified and those that are not. Although the specification teaches conventional screening protocols to identify homologs and polymorphic variants of PRC17 which can be used as diagnostic tools (p. 25, lines 8-24), these conventional assays do not remedy the deficiencies of the specification drawn to the broadly claimed variants to be assayed or satisfy the requirements of 35 USC 112, first paragraph. Applicant is reminded that 35 USC 112, first paragraph does not require that the specification teach how to screen for polynucleotides to be assayed, but rather

requires that the specification teach how to make and use the claimed invention. In particular, screening assays do not enable the claimed invention because the court found in (*Rochester v. Searle*, 358 F.3d 916, Fed Cir., 2004) that screening assays are not sufficient to enable an invention because they are merely a wish or plan for obtaining the claimed chemical invention. It is clear that the specification does provide the necessary guidance to one of skill to enable the making of the claimed invention, that is the ability to predictably distinguish between those genes that are overexpressed and/or amplified from those that are not. Since the making of the broadly claimed invention is not enabled, one would not know how to use the broadly claimed invention in the absence of specific information drawn to overexpressed and/or amplified genes that encode SEQ ID NO:2.

The specification provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predictably distinguish the claimed gene to be assayed so that the invention could function as claimed with a reasonable expectation of success. In the absence of guidance or exemplification so that the broadly claimed assayable gene could be predictably made, the screening assays taught are drawn only to a wish or a plan for making the claimed invention. For the above reasons, it appears that undue experimentation would be required to enable one to practice the claimed invention.

6. Claims 1-9 are rejected under 35 USC 112, first paragraph, as lacking an adequate written description in the specification.

Claims 1-9 are drawn to a method of detecting cancer cells in a biological sample from a mammal comprising detecting a nucleic acid molecule encoding a PRC17 polypeptide comprising at least 85% amino acid identity to an amino acid

sequence of SEQ ID NO:2, wherein an increase in the level of the nucleic acid molecule in the sample compared to normal indicates the presence of cancer cells. This means detecting cancer cells by detecting a nucleic acid molecule that encodes a PRC17 polypeptide, wherein said PRC17 polypeptide is defined by the specification as including polymorphic variants, mutants, interspecies homologs that have at least 85% identity to a region of about 20 or more amino acids of SEQ ID NO:2 (p. 26), wherein it is noted that the specification does not require that the amino acids be contiguous and which means that a PRC17 polypeptide is any polypeptide with 17 amino acids in common with PRC17 over a range of 20 amino acids. It is noted that the specification does not establish a nexus between a polynucleotide encoding SEQ ID NO:2 and either overexpression of amplification of PRC17 in cancer cells.

Although drawn to DNA arts, the findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." Id. At 1567, 43 USPQ2d at 1405. The court also stated that

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully

described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that "the written description requirement can be met by 'show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. " Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to claims such as those at issue here. A

disclosure that does not adequately describe a product itself logically cannot adequately describe a method of using that product.

Thus, the instant specification may provide an adequate written description of the polynucleotides encoding polymorphic variants, mutants, interspecies homologs that have at least 85% identity to a region of about 20 or more amino acids of SEQ ID NO:2 or a polynucleoetide encoding SEQ ID NO:2 that will function as claimed, per Lilly by structurally describing a representative number of polynucleotides encoding, polymorphic variants, mutants, interspecies homologs that have at least 85% identity to a region of about 20 or more amino acids of SEQ ID NO:2 or a polynucleotide encoding SEQ ID NO:2 that will function as claimed or by describing "structural features common to the members of the genus, which features constitute a substantial portion of the genus." Alternatively, per Enzo, the specification can show that the claimed invention is complete "by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics."

In this case, the specification does not describe the polynucleotides encoding polymorphic variants, mutants, interspecies homologs that have at least 85% identity to a region of about 20 or more amino acids of SEQ ID NO:2 or polynucleotide encoding SEQ ID NO:2 that will function as claimed in a manner that satisfies either the Lilly or Enzo standards. In particular, the specification does not provide the complete structure of any polynucleotide encoding SEQ ID NO:2 that will function as claimed since there is no nexus provided in the specification between a polynucleotide encoding SEQ ID NO:2 and either amplification or overexpression of the encoding polynucleotides in cancer cells or the complete structure of any

polynucleotides encoding polymorphic variants, mutants, interspecies homologs that have at least 85% identity to a region of about 20 or more amino acids of SEQ ID NO:2 that will function as claimed, nor does the specification provide any partial structure of such polynucleotides that will function as claimed, nor any physical or chemical characteristics of the polynucleotides nor any functional characteristics coupled with a known or disclosed correlation between structure and function. Although the specification discloses that an unidentified polynucleotide encoding a PRC17 polypeptide is overexpressed and/or amplified in a variety of primary cancer cells, this does not provide a description of the claimed polynucleotides that would satisfy the standard set out in Enzo.

The specification also fails to describe the polynucleotides encoding polypeptides, polymorphic variants, mutants, interspecies homologs that have at least 85% identity to a region of about 20 or more amino acids of SEQ ID NO:2 or polynucleotide encoding SEQ ID NO:2 that will function as claimed by the test set out in Lilly. The specification describes only a single unidentified polynucleotide, encoding a PRC17 polypeptide, that is overexpressed and/or amplified in a variety of cancer cells. Therefore, it necessarily fails to describe a "representative number" of such species. In addition, the specification also does not describe "structural features common to the members of the genus, which features constitute a substantial portion of the genus."

Thus, the specification does not provide an adequate written description of either the polynucleotides encoding polymorphic variants, mutants, interspecies homologs that have at least 85% identity to a region of about 20 or more amino acids of SEQ ID NO:2 or the polynucleotide encoding SEQ ID NO:2 that is required to practice the claimed invention. Since the specification fails to adequately describe

the product which is assayed to detect cancer cells, it also fails to adequately describe the method using the product.

7. Claims 4-5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. Claims 4-5 are indefinite because claim 4 recites the phrase "the gene" and there is no antecedent basis for "the gene" in claim 3 from which claim 4 depends

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1-5, 9 are rejected under 35 U.S.C. § 102(b) as being anticipated by Onno et al (DNA and Cell Bio., 1993, 12:107-118, IDS item.

The claims are drawn to a method of detecting cancer cells in a biological sample from a mammal comprising detecting a nucleic acid molecule encoding a PRC17 polypeptide comprising at least 85% amino acid identity to an amino acid sequence of SEQ ID NO:2, wherein an increase in the level of the nucleic acid molecule in the sample compared to normal indicates the presence of cancer cells (claim 1), wherein the polypeptide has an amino acid sequence of SEQ ID NO:2 (claim 2), wherein the detecting step further comprises contacting the nucleic acid molecule with a probe under conditions which the probe selectively hybridizes to the nucleic acid molecule to form a stable hybridization complex (claim 3), wherein the contacting step further comprises a step of amplifying the gene in an amplification

reaction (claim 4), a PCR reaction (claim 5), wherein the mammal is a human (claim 9).

It is noted that since claim 2 is drawn to detection of a nucleic acid encoding an amino acid sequence of SEQ ID NO:2, thus it is assumed for examination purposes that the claim is drawn to detecting a nucleic acid that encodes at least 2 consecutive amino acids of SEQ ID NO:2 and that the nucleic acid detected is not limited to a sequence encoding SEQ ID NO:2.

Onno et al teach a method of detecting Ewing sarcoma cancer cells in a biological sample from a mammal comprising detecting a nucleic acid molecule encoding a PRC17 polypeptide comprising at least 85% amino acid identity to an amino acid sequence of SEQ ID NO:2, wherein an increase in the level of the nucleic acid molecule in the sample compared to normal indicates the presence of cancer cells since the gene is found in Ewing sarcoma cancer cells but not in normal somatic cells (see abstract), wherein the detecting step further comprises contacting the nucleic acid molecule with a probe under conditions which the probe selectively hybridizes to the nucleic acid molecule to form a stable hybridization complex (page 109, para bridging columns 1 and 2), wherein the polypeptide has an amino acid of SEQ ID NO:2 (see Figure 3 wherein the differences between TRE17 wt and TRE17 onc coding sequences are disclosed wherein it is clear that TRE17 onc encodes a PRC17 polypeptide comprising at least 85% amino acid identity to an amino acid sequence of SEQ ID NO:2 , it is noted that TRE17 wt has 100% identity to SEQ ID NO:2, see Attached Appendix 1), wherein the detecting step further comprises contacting the nucleic acid molecule with a probe under conditions which the probe selectively hybridizes to the nucleic acid molecule to form a stable hybridization complex, wherein the contacting step further comprises a step of amplifying the gene in an

amplification reaction, a PCR reaction (see columns 1 and 2 of page 109, "DNA amplification by the polymerase chain reaction), wherein the mammal is a human (see page 113, col 1).

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 1, 6-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Onno et al, *Supra* in view of Pollack et al, *Supra*.

The claims are drawn to a method of detecting cancer cells in a biological sample from a mammal comprising detecting a nucleic acid molecule encoding a PRC17 polypeptide comprising at least 85% amino acid identity to an amino acid sequence of SEQ ID NO:2, wherein an increase in the level of the nucleic acid molecule in the sample compared to normal indicates the presence of cancer cells (claim 1), wherein the nucleic acid is an mRNA (claim 7), wherein the biological sample is a tissue biopsy (claim 8), wherein the cancer cells are selected from the group consisting of prostate tissue, breast tissue, lung tissue and ovarian tissue (claim 8).

Onno et al teach as set forth above but do not teach the method wherein the nucleic acid is an mRNA, wherein the biological sample is a tissue biopsy, wherein

the cancer cells are selected from the group consisting of prostate tissue, breast tissue, lung tissue or ovarian tissue.

Pollack et al teach that gene amplifications frequently contribute to tumorigenesis. Characterization of DNA copy-number changes is important for both the basic understanding of cancer and its diagnosis. The reference describes a cDNA microarray-based CGH method and its application to DNA copy-number variation analysis wherein analysis in breast cancer tumors (that is biopsy samples see p. 44, col 2) is exemplified, wherein gene amplifications were identified genome-wide and with high resolution and sensitive comparisons were made between alterations in DNA copy number and gene expression, that is mRNA expression was assessed (see abstract and Figure 1, pages 41). The cDNA microarray measurements of DNA copy number were reproducible and displayed both greater dynamic range and higher resolution than has been previously reported (p. 44, col 1). Pollack et al further teach that not all amplified genes are highly expressed (p. 45, col 1).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to substitute the Ewing Sarcoma sample of Onno et al for the breast cancer sample of Pollack et al in the method of Pollack et al in order to detect cancer cells in a biological sample comprising assaying for both the nucleotide encoding and the mRNA expressed by said polynucleotide given the specific teaching in Onno et al that the detected gene is overexpressed in Ewing Sarcoma cells as compared with normal cells. One would have been motivated to detect both amplification and mRNA expression in order to determine if the assay of mRNA would be useful for detecting Ewing Sarcoma, given the teaching of Pollack et al that not all amplified genes are highly expressed. Thus if it were to be discovered the mRNA is overexpressed, this would broaden the assays available for diagnostic

testing. Further, one would have been motivated to assay cancer biopsy tissue samples from prostate tissue, breast tissue, lung tissue and ovarian tissue or any other cancer type to determine if these cancer types also amplify the nucleotide encoding and/or the expressed mRNA in order to determine whether any of these tumor types can be detected by assay with a probe that selectively hybridizes to the nucleic acid molecule of Onno et al.

13. No claims allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Ungar, PhD whose telephone number is (571) 272-0837. The examiner can normally be reached on Monday through Friday from 7:30am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached at (571) 272-0787. The fax phone number for this Art Unit is (571) 273-8300.

Susan Ungar
Primary Patent Examiner
February 9, 2005